EDITORIAL COMMENT

Diagnosing Acute Heart Failure

The Mathematician and the Clinician*

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For giving us a glimpse of the inevitable future, Steinhart et al. (1) deserve credit. In this issue of the Journal, the authors have created a mathematical diagnostic prediction model for assessing the likelihood of the presence of acute heart failure (AHF) by combining clinical assessment and measurement of N-terminal pro-B-type natriuretic peptide (NT-proBNP). Pre-test clinical assessment of the likelihood of AHF and the NT-proBNP result are included in the entered information. The model is explained well. It evaluates the clinical assessment as a categorical variable and the NT-proBNP data as a continuous variable. The model was validated internally against the adjudicated diagnoses in 534 patients from the IMPROVE-CHF (Improved Management of Patients With Congestive Heart Failure) study (2) and externally in data from 573 patients from the PRIDE (N-Terminal Pro-BNP Investigation of Dyspnea in the Emergency Department) study (3). The article demonstrates that the model has excellent diagnostic accuracy, especially in cases of intermediate clinical probability. In these patients, the model appropriately reclassified the likelihood to either low or high probability of AHF with negligible inappropriate redirection.

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Let us get back for a moment to the emergency department. What do clinicians do when a patient presents with acute dyspnea? We observe the patient, interview the patient and family, take a history, and perform a physical examination. We try to elicit symptoms suggestive of AHF, detect signs indicating congestion, and search for objective evidence of a structural or functional abnormality of the heart at rest. Common cardiovascular and noncardiovascular comorbidities that may contribute to the clinical symptoms should be identified. The initial routine investigations, which usually include electrocardiogram, blood gases, chest X-ray, and hopefully echocardiography, are evaluated.

The patient’s response to initial management frequently determines subsequent treatment. When the laboratory data arrive, we look for evidence of contributory factors such as anemia, infection, renal dysfunction, or acute coronary syndrome. If we are lucky, we get a natriuretic peptide level quickly. We know that the levels of this biomarker contain important diagnostic and prognostic information and the greater the value, the more likely the diagnosis of HF. Often the diagnostic workup and treatment algorithm will proceed simultaneously.

The clinician will enter all of this information into his or her cortex and assimilate it by a complex neurologic process that occurs on both conscious and subconscious levels. Experience and knowledge will determine the success of the operation, which represents a sophisticated biologic data-management process that results in a prediction of the likelihood of the presence of AHF.

Why is diagnosing AHF so difficult? Most definitions of AHF emphasize the rapid-onset aspect of the symptoms and the need for urgent therapy (4), but it is a mixed bag of patients. The etiologies are heterogeneous, with ischemic heart disease and hypertension dominating, and mildly elevated troponins are frequently observed. The impact on dyspnea of comorbidities such as pulmonary disease, infection, anemia, or renal dysfunction can be challenging to assess. The fact that so many patients have a preserved ejection fraction, with or without objective findings that suggest diastolic function, complicates confirmation of the diagnosis. Much of the information we have in AHF is subjective, qualitative, and variable between patients and hospitals. Obviously, clinical skills also may vary considerably among physicians.

The data on natriuretic peptides have been collected from heterogeneous patient cohorts. Studies have sampled natriuretic peptides from patients presenting with increasing dyspnea to their primary care physician and to the hospital, including patients with known chronic heart failure who decompensate acutely or who present for the first time with new onset AHF. The data on this biomarker stem from diverse groups. There is no consensus concerning cutoff levels (5). The strongest documented evidence relates to the negative predictive value; low levels of natriuretic peptides make the diagnosis of heart failure unlikely. However, during “flash” pulmonary edema, natriuretic peptide levels may remain normal at the time of admission.

Anecdotes sometimes are illustrative. A few weeks ago I recruited a patient admitted with acute dyspnea for an AHF trial. He was 65 years of age with a rapid onset shortness of breath over a few hours with no chest pain. He had a history of a single uncomplicated anterior myocardial infarction and had been essentially asymptomatic. On admission we recorded sinus tachycardia, tachypnea, and a blood pressure of 180/95 mm Hg. His hemoglobin saturation was 88% on 2 l
of oxygen in the emergency department. He had bilateral rales half-way up the lung fields, and chest X-ray confirmed pulmonary edema. The echocardiogram showed a good left ventricle with only mild left ventricular dilation and an ejection fraction of 45%. Two troponins were \(<0.05 \mu g/l\). He was responding well to intravenous morphine, furosemide, nitroglycerin, and a continuous positive airway pressure mask. He had just consented to participate in the trial when the NT-proBNP appeared on the laboratory screen. It was 150 pmol/l. The natriuretic peptide level was too low and he was therefore excluded from the trial. Alas, I lost my otherwise “perfect” patient.

The lack of objective criteria can make determination of sample size and event rate in randomized clinical trials difficult. Inclusion of patients without AHF can dilute treatment effect and potentially reduce the trial’s power to detect the effect of intervention. Including BNP measurement as an inclusion criterion would assure a cohort with a more certain diagnosis and greater number of cause-specific end points. There may well be a useful role for a mathematical model in determining sample size for a randomized clinical trial. However, in clinical practice do we need an innovative diagnostic model that will integrate natriuretic peptide levels with clinical evaluation?

What do we essentially need to know when evaluating a patient with acutely progressive dyspnea: The critical clinical question must be to determine whether there is pulmonary congestion. Which is worse: to treat a patient for AHF who does not have heart failure or to delay treatment of a patient with AHF? Delaying treatment is not a good alternative, especially when initial management options such as oxygen, diuretics, morphine, and noninvasive ventilation should not usually be detrimental in patients without AHF or pulmonary congestion. Clinicians charged with the responsibility of managing a patient with acute dyspnea should be able to make a decision based on the history, physical examination, blood gases, and chest X-ray.

The reader of the paper by Steinhart et al. (1) should be aware of some important limitations. The most common etiology in patients with AHF is an acute coronary syndrome. Those patients, as well as patients with infection, obstructive airways disease, or moderate renal dysfunction were excluded from the 2 patient cohorts used to evaluate the model. Such selected populations seriously limit the applicability of the results. Another major limitation concerns the “gold standard” diagnosis. Those of us who have worked on adjudication committees know how challenging the process can be in AHF trials, and unanimous consensus is not always easily obtained. The interested reader should understand these deliberations in detail and know specifically what information was requisite for the final diagnosis of AHF, especially so when the accuracy of a redirection for the presence or absence of AHF is necessarily dependent on subjective adjudication. The strength of the continuous model as compared with one with multiple categories for the predictors is not obvious. Is it not possible that several categories of pre-test estimated probability and NT-proBNP levels might be as reliable as continuous variables? It would certainly be easier to apply in practice.

Clinical skills are judged by our ability to collect, weigh, and correctly interpret all of the available information. I believe that we do evaluate all of this information in both categorical and continuous fashions. Someday a software program will outperform a good clinician. It will be the end of an era, but perhaps the dawn of a new epoch.

**Key Words:** acute heart failure • diagnosis • natriuretic peptide • prediction model • Bayesian theorem.

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**REFERENCES**

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